Increasing fMRI Specificity using Asymmetric Spin Echo (ASE) Spiral: An ROC-based Analysis

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Introduction: When studying brain function, both the *sensitivity* and *specificity* of a technique are essential for improving accuracy. Most fMRI studies use sequences with T_2' weighting to maximize BOLD sensitivity, but this often comes at a cost to specificity as these sequences detect activation in draining veins far from the site of neural activation [1]. T_2-weighted sequences have been shown to be more specific to "true" BOLD activation within parenchymal tissue, but with the trade-off of being far less sensitive [2].

The objective of this study was to examine whether ASE Spiral is a better compromise for balancing sensitivity and specificity. Using the ASE Spiral technique [3] it is possible to acquire, in a single RF excitation, three images with matched T_2'-weighting, and varying T_2-weighting. Therefore, ASE Spiral acquires three images with equivalent BOLD weighting. In this work, we analyzed ASE Spiral images obtained during visual checkerboard stimulus using a Receiver-Operator-Characteristic (ROC)-based analysis [4], to study changes in specificity as a function of varying relaxation weighting.

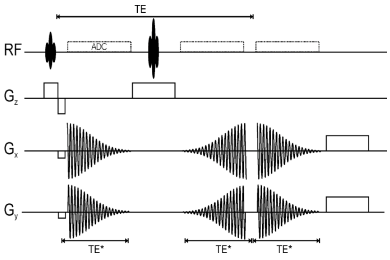

Figure 1 - ASE Spiral sequence, showing acquisition of 3 spiral images per excitation.

Methods: All data were obtained using a 4T Varian INOVA whole body MRI, using a body gradient set operated at a maximum amplitude and slew rate of 35.5 mT/m and 120 T/s, respectfully. For each sequence-type, fMRI experiments using an alternating radial checkerboard with a total visual angle of 9.53° (5 visual stimulation periods and 4 rest periods, each with 20 s duration) were used to elicit activation in the visual cortex. Data were acquired from 12 healthy subjects (mean age = 23.6, SD=4.12), and four 3-mm axial slices per volume (covering the primary visual cortex) using 128x128, 4-shot, 24 cm FOV, 2s TR. Three sequences were compared for each subject (with counter-balanced ordering): Spiral-In/Out [5] (TE = 30 ms, flip = 60°), Spin-Echo-In/Out (TE = 105ms) and the ASE Spiral sequence (TE = 75 ms, $TE^*_1 = TE^*_2 = TE^*_3 = 30$ ms). A venogram was also acquired for the same slices (3mm thick, 0.5 mm gap), 256x256, min TR, TE=30ms, 20° flip.

FMRI statistical analyses and activation maps were calculated using the fMRI Expert Analysis Tool (FEAT) Version 5.63 in FSL [6]. Activation maps were thresholded using clusters determined by Z>2.3 and a (corrected) cluster significance threshold of P=0.05. The fMRI activation was also overlaid on the venogram to examine whether functional activation was localized to veins. Specificity maps were generated based on an ROC analysis using the number of active voxels located on veins as the activation threshold was varied. Results are shown for individual subjects only.

Specificity is equal to TN/(FP + TN), where FP = number of false positives (activation on veins), TN = number of true negatives (veins with no activation). The "faster" a specificity curve reaches a value of 1.0, the more specific the activation is to tissue as opposed to a draining vessel.

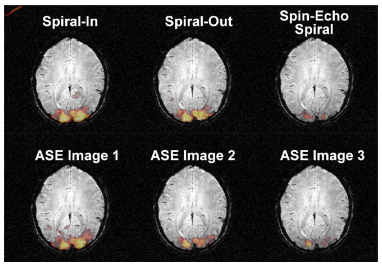

Figure 2 - FMRI activation from a checkerboard task, overlaid on a venogram. Z-scores range from 2.3-12.

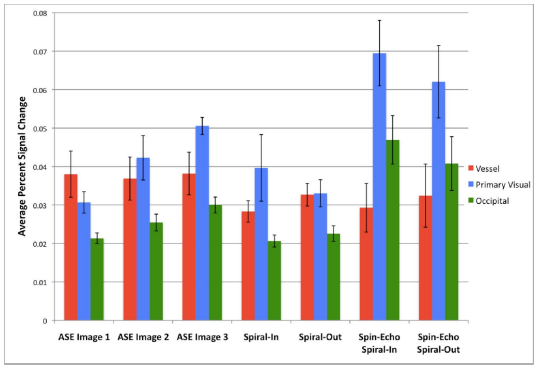

Figure 3 - Percent signal change for visual activation in several ROIs for individual ASE and gradient and spin-echo images.

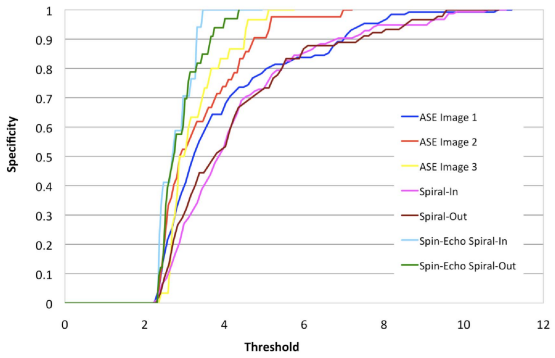

Figure 4 - Individual image specificity curves as a function of activation threshold. Specificity = TN/(FP+TN).

Results & Discussion: As expected, Spiral-In and Spiral-Out acquisition had an activation pattern and extent that was comparable to that of the first ASE image (see Figure 2). Activation results seen in all three of these maps include both neural and vascular origins. The third ASE image resulted in an activation pattern and extent that corresponded most closely to the purely T_2-weighted spin-echo acquisition (Figure 2). Activation clusters remaining for ASE image 3 were localized to the primary visual cortex.

The three ASE images had increasing percent signal change in the visual cortex, however, the percent signal change remained consistent for all ASE images in vessels (Figure 3). These results are consistent with previous work [2], in which T2-weighted fMRI exhibited increasing sensitivity to neural BOLD activity relative to vascular BOLD. This reflects the increasing contribution of T_2-weighting in the latter ASE images (although equivalent T_2'-weighting), and introduces the potential that these images may be combined in such as way as to increase the specificity relative to the pure BOLD effect observed in the first ASE image.

A more direct analysis of specificity was performed using an ROC-based analysis (described above), using the venogram to identify true negatives and false positives. Specificity curves for a representative subject are shown in Figure 4 for all individual images types obtained (ASE, SE-Spiral-In/Out, conventional Spiral-In/Out). As expected, the highest specificity is observed for the purely T_2-weighted images, and the lowest specificity is observed for the pure T_2*-weighted images. ASE images were shown to trend as a function of image number. The first ASE image has specificity similar to that of Spiral-In and Spiral-Out. Later ASE images have increasing specificity approaching that of the Spin-Echo images. Group data confirms that the specificity of the three ASE images significantly increases as a function of T_2-weighting (t = 2.1E-05, df = 11, paired).

Conclusions: Although sensitivity does decrease with ASE image number (in extent and z-scores), the percent signal change actually increases in visual cortex in later ASE spiral images. Specificity also increases with ASE image number. Later ASE images are more specific than standard BOLD spiral images, but less specific than a pure Spin-Echo image. The ability to obtain images with matched BOLD-weighting and increasing T_2-weighting during the same acquisition is a novel feature of the ASE sequence. By combining individual ASE images, we can utilize both the improved specificity of later images with the stronger sensitivity of earlier images.

References: **[1]** J. Gati *et al. Magn Reson Med* **38** 296-302 (1997) **[2]** T Duong *et al. Magn Reson Med.* **49** 1019-1027 (2003). **[3]** KD Brewer *et al. NMR in Biomed.* **22** 654-662 (2009). **[4]** D. Shapiro *Stat Methods Med Res* **8** 113-134 (1999) **[5]** G.H. Glover & C.S. Law. *Magn Reson. Med.* **46** 515-522 (2001). **[6]** S.M. Smith *et al. NeuroImage* **23** 208-219 (2004).